

# Risk Factors for Tissue and Wound Complications in Gastrointestinal Surgery

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**Background:** Surgical site infections and disruption of sutured tissue are frequent complications following surgery. We aimed to assess risk factors predictive of tissue and wound complications in open gastrointestinal surgery.

**Methods:** Data from 4855 unselected patients undergoing open gastrointestinal surgery from 1995 through 1998 were recorded in a clinical database and validated. The database embraced variables related to patient history, preoperative clinical condition, operative findings and severity, and the surgeon's training. Variables predictive of surgical site infection and dehiscence of sutured tissue within 30 days after surgery were assessed by multiple logistic regression analysis.

**Results:** Following elective operation, the incidence of tissue and wound complications was 6% compared with 16% in emergency surgery ( $P < 0.001$ ). These complications resulted in prolonged hospitalization in 50% of the patients and a 3-fold higher risk of reoperation but not increased mortality. Factors associated with complications following elective operations were smoking, comorbidity, and perioperative blood loss. Following emergency operations, male gender, peritonitis, and multiple operations were predictors of complications. Irrespective of elective or emergency surgery, the type of operation was a predictor of complications.

**Conclusion:** Factors known to affect the process of tissue and wound healing are independently associated with tissue and wound complications following gastrointestinal surgery.

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Surgical site infections and wound and tissue dehiscence are well-known postoperative complications in gastrointestinal surgery. The severity of these complications em-

braces mild cases needing local wound care and antibiotics to serious cases with multiple reoperations and a high mortality rate. In most cases, such complications prolong hospitalization, with a substantial increase in cost of care.<sup>1,2</sup>

Traditionally, local factors such as the degree of contamination and the surgical technique have been regarded as strong predictors for surgical site infection and wound dehiscence.<sup>3,4</sup> More recent studies, however, have disregarded the significance of surgical technique, and others have identified systemic factors such as high age, gender, lifestyle, and coexisting morbidity as playing a significant role in the pathogenesis of these complications.<sup>5,6</sup>

To audit surgical outcome, a clinical database for operative risk and complications was established in 1994 at the Department of Surgical Gastroenterology, Bispebjerg Hospital.<sup>7</sup> The database embraced variables related to the patient and lifestyle factors, characteristics of the disease, the patients' preoperative condition, operative severity and findings, and the surgeon's level of training.

The aim of this study was to identify and assess factors predictive of postoperative tissue and wound complications when adjusting for potential confounders through multiple logistic regression analysis.

## MATERIALS AND METHODS

From January 1995 through December 1998, a cohort of 4855 consecutive patients operated on for gastrointestinal disease was evaluated. The operations were performed at the Department of Surgical Gastroenterology, Bispebjerg Hospital, and included herniotomy, gastric, duodenal, pancreatic, and biliary surgery, as well as operations on the small bowel, appendix, colon, and rectum. Laparoscopic, anal, and perianal operations were excluded.

Variables as listed in Table 1, with possible relation to postoperative complications, were assessed. Data regarding patient history (family status, employment and functional dependent status, smoking and drinking habits, and comorbidity [defined as a medical disease in current treatment]) were collected from questionnaires completed prior to oper-

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TABLE 1. Baseline Characteristics\*

	Elective Operations n = 3388	Emergency Operations n = 1867
Anamnestic variables		
Age (median, interquartile range)	61 (46–74)	61 (32–77)
Male gender	2043 (60.3)	887 (47.5)
Family status (single or widow)	1216 (35.9)	867 (46.4)
Employed	1244 (36.7)	528 (28.3)
Dependent functional status	258 (7.6)	343 (18.4)
Smoker	1403 (41.4)	791 (42.4)
Alcohol abuser (more than 5 drinks per day)	141 (4.2)	101 (5.4)
Diabetes, cardiovascular disease, or lung disease	1074 (31.7)	646 (34.6)
Liver cirrhosis or previous myocardial infarction or stroke	231 (6.8)	175 (9.7)
Physiologic variables		
Systolic blood pressure (<110 or >130 mm Hg)	402 (11.9)	241 (12.9)
Pulse (<50 or >80 beats per minute)	1109 (32.7)	1007 (53.9)
Electrocardiogram (not sinus rhythm)	166 (4.9)	175 (9.4)
Hemoglobin (<6.8 or >10.2 mmol/L) <sup>†</sup>	235 (6.9)	336 (18.0)
Leucocyte count (>10.1 or <4.0 billion/L) <sup>†</sup>	190 (5.6)	1078 (57.7)
P-Kalium (<3.5 or >5.0 $\mu$ mol/L) <sup>†</sup>	219 (6.5)	460 (24.6)
P-Natrium (<135 $\mu$ mol/L) <sup>†</sup>	169 (5.0)	346 (18.5)
P-Creatinine (>125 $\mu$ mol/L) <sup>†</sup>	108 (3.2)	225 (12.1)
Operative variables		
Hernia surgery	1915 (56.5)	130 (7.0)
Gallbladder surgery	666 (19.7)	122 (6.5)
Gastric or duodenal surgery	63 (1.9)	233 (12.5)
Intestinal surgery	139 (4.1)	453 (24.3)
Appendix surgery	0 (0.0)	647 (34.7)
Colon or rectum surgery	578 (17.1)	285 (15.3)
Operative severity (difficult or very difficult)	593 (17.5)	528 (28.3)
Multiple operations	220 (6.5)	287 (15.4)
Blood loss (>100 mL)	750 (22.1)	662 (35.5)
Peritonitis (serous fluid, local, or diffuse)	57 (1.7)	566 (30.3)
Malignancy	511 (15.1)	222 (11.9)
Specialist surgeon	1232 (36.4)	308 (16.5)
Reoperation	182 (5.4)	234 (12.5)

\*Values are number of operations (with percentages in parentheses) unless stated in brackets.

<sup>†</sup>Values deviating from reference interval.

ation by the patient or surgeon at admission or at referral to the outpatient clinic. These data and data from the operation and clinical record were recorded on a database sheet by the surgeon pre- or postoperatively.

Postoperative tissue and wound complications were defined as surgical-site infections (superficial or deep wound infection, wound abscess, or intraabdominal abscess) or disruption of sutured tissue (wound, fascia, or anastomosis). At discharge, the surgical staff recorded complications and reoperations. Complications occurring after discharge, but within 30 days after surgery, were recorded on readmission. In case of admission to other departments of the hospital within 30 days, relevant data were extracted from retrieved clinical records and discharge letters. Thus, only complications needing hospitalization were recorded.

The data were entered in the database by use of the EPI-INFO 6.0 software (Centers for Disease Control and Prevention, Atlanta, GA). Entry of data on all patients was ensured by continual control procedures.<sup>7</sup> In addition, data from operations performed during 1995 through 1996 (n = 2036) were validated by use of the software to select cases containing logical errors and subsequently to correct the errors by matching the data with the clinical record. Data from operations performed during 1997 through 1998 (n = 3260) were validated manually by matching the data with the clinical record.

The data were analyzed by multiple logistic regression using the SAS 8.02 software (SAS Institute Inc., Cary, NC). Separate analyses were conducted on elective and emergency operations, with postoperative wound complications as the dependent variable. As the database embraced patients operated on more than once, generalized estimating equations were used to adjust for dependent complications occurring in patients undergoing surgery more than once.

In each analysis, a univariate analysis was performed, with “patient age” and “gender” as fixed covariates. A linear spline function was used to check if the assumption of linearity in the continuous variable “patient age” was fulfilled. This was the case in models involving elective operations, but in the models of emergency operations nonlinearity was found, and “patient age” was modeled as piecewise linear accordingly.

Based on these univariate models, the odds ratio of each variable was estimated. The multivariate models were achieved by a forward selection procedure where variables likely to be associated with outcome ( $P \leq 0.2$ ) were included. In these models, all variables not significantly associated with outcome ( $P > 0.05$ ) were discarded by backward elimination. Finally, interaction terms between the variables were examined. All results were described with odds ratio and 95% confidence interval.

## RESULTS

A total of 5296 operations entered the database, of which 3388 (64.4%) were elective and 1867 (35.5%) emergency operations. Forty-one operations (0.8%) were discarded due to missing patient identification numbers. The overall incidence of tissue and wound complications was 6% following elective operation (Table 2), and 44% of these patients (89/277) were admitted for more than 15 days after surgery. Following emergency operation, 16% had a tissue or wound complication (Table 2), and 52% (159/348) were admitted for more than 15 days following surgery. Tissue and wound complications were not independently associated with postoperative mortality.

The analysis of factors associated with tissue and wound complications following elective surgery disclosed that smoking, comorbidity, perioperative blood loss, and type of operation were independent predictors (Table 3). Multivariate subgroup analysis of the association between smoking

**TABLE 2.** Postoperative Tissue and Wound Complications\*

	<b>Elective Surgery n = 8388</b>	<b>Emergency Surgery n = 1867</b>	<b>P Value<sup>†</sup></b>
<b>Surgical site infections</b>			
Superficial wound infection	69 (2.0)	90 (4.8)	
Deep wound infection	47 (1.4)	60 (3.2)	
Intraabdominal abscess	41 (1.2)	84 (4.5)	
Total	157 (4.6)	234 (12.5)	
One or more surgical-site infections	144 (4.3)	208 (11.1)	<0.001
<b>Wound or tissue disruption</b>			
Wound or fascial rupture	29 (0.9)	70 (3.7)	
Anastomotic leakage	51 (1.5)	72 (3.9)	
Total	80 (2.4)	142 (7.6)	
One or more wound or tissue disruptions	77 (2.3)	135 (7.2)	<0.001
<b>Tissue and wound complications</b>			
Total	237 (7.0)	376 (20.1)	
One or more tissue and wound complications	202 (6.0)	305 (16.3)	<0.001

\*Values are number of operations (with percentages in parentheses).

<sup>†</sup> $\chi^2$  (2-sided).

**TABLE 3.** Variables Associated With Tissue and Wound Complications Following Elective Operation Analyzed by Logistic Regression: The Final Model\*

	<b>Univariate</b>		<b>Multivariate</b>	
	<b>OR</b>	<b>95% CI</b>	<b>OR</b>	<b>95% CI</b>
<b>Smoking status</b>				
Nonsmoker	1	—	1	—
Smoker	1.73	1.26–2.36	1.76	1.27–2.43
<b>Comorbidity<sup>†</sup></b>				
No	1	—	1	—
Yes	1.41	1.00–1.99	1.47	1.45–2.07
<b>Blood loss</b>				
<100 mL	1	—	1	—
100–500 mL	3.35	2.24–5.05	1.70	1.00–2.91
>500 mL	8.75	5.87–13.02	3.82	2.19–6.68
<b>Operation</b>				
Hernia surgery	1	—	1	—
Biliary surgery	0.98	0.52–1.87	0.83	0.43–1.59
Gastroduodenal surgery	3.48	1.13–10.71	2.07	0.58–7.40
Small-bowel surgery	4.42	2.31–8.44	2.84	1.41–5.70
Colorectal surgery	7.08	4.70–10.68	3.21	1.79–5.74

\*Cases included in the model: 3148; cases rejected due to missing data: 217.

<sup>†</sup>Diabetes, cardiovascular disease, or lung disease. Variables significantly associated with tissue and wound complications in the univariate analysis, but failed to be significant in the final multivariate model were family status, multiple operations, malignancy, reoperation, and surgeon's training.

and complications disclosed that smoking was independently associated with surgical site infections (OR 1.64; 1.13–2.38), as well as tissue and wound dehiscence (OR 1.80; 1.02–3.16). In emergency surgery, male gender, peritonitis, operation, and multiple operations were independent predictors of tissue and wound complications (Table 4).

The association between complications and perioperative blood loss disclosed a significant dose-relationship, signifying that a large blood loss yielded a higher risk of complications.

## DISCUSSION

This study demonstrates a significantly higher incidence of postoperative tissue and wound complications in emergency than elective surgery, thus confirming previous reports.<sup>8–12</sup> When present, infection and disruption of wounds and tissues were associated with a higher risk of reoperation and a prolonged postoperative admission.<sup>13</sup> Opposite other reports, no association between wound complications and mortality was found.<sup>13</sup>

Common for all tissues subject to surgery is disruption of the local vascular supply, thrombosis of the vessels, and tissue hypoxia.<sup>14</sup> Once the blood supply is restored, several

**TABLE 4.** Variables Associated With Tissue and Wound Complications Following Emergency Operation Analyzed by Logistic Regression the Final Model\*

	Univariate		Multivariate	
	OR	95% CI	OR	95% CI
Gender				
Female	1	—	1	—
Male	1.43	1.07–1.89	1.46	1.10–1.94
Peritonitis				
None	1		1	
Serous fluid	1.06	0.73–1.53	0.84	0.57–1.23
Localized pus	2.38	1.60–3.54	2.06	1.34–3.18
Diffuse	2.98	2.05–4.34	1.86	1.24–2.81
Operation				
Hernia surgery	1	—	1	—
Appendix surgery	2.01	0.91–4.47	1.64	0.72–3.77
Biliary surgery	2.17	0.90–5.25	1.90	0.76–7.74
Gastroduodenal surgery	3.38	1.57–7.30	2.59	1.15–5.85
Small-bowel surgery	4.03	1.91–8.46	2.83	1.30–6.15
Colorectal surgery	6.90	3.28–14.51	4.88	2.23–10.72
Multiple operations				
1 Operation	1		1	
>1 Operation	2.95	2.12–4.10	2.32	1.63–3.28

\*Cases included in the model: 1847; cases rejected due to missing data: 23.

Variables significantly associated with tissue and wound complications in the univariate analysis but failed to be significant in the final multivariate model were pulse, impaired sensorium, blood loss, malignancy, reoperation, and surgeon's training.

factors may complicate healing. The most important seems to be proliferation of bacteria in the wound and tissue, which affects each process involved in healing and increases the risk of wound infection, delayed healing, and dehiscence.<sup>15</sup>

In both elective and emergency surgery, large operations like colorectal and small-bowel operations were more strongly associated with complications than smaller operations. Wound infections, intraabdominal abscesses, and anastomotic leakage are known to occur more frequent following surgery on the lower than upper gastrointestinal tract.<sup>16,17</sup> This observation is presumably due to the higher incidence of anastomotic dehiscence of colon and especially rectal anastomoses, where the intraluminal bacterial load is high.<sup>8,18</sup> Presence of bacteria in the healing tissue affects all processes of healing and promotes impairment of collagen synthesis and release of proteolytic enzymes, which promotes dehiscence by decreasing the suture-holding capacity of the tissue.<sup>19</sup>

Following elective operations, perioperative blood loss was a predictor of postoperative tissue and wound complications in a dose-dependent manner, when adjusting for other risk factors and confounders. This finding confirms previous

reports<sup>6,20</sup> and suggests that hypovolemia and reduction of tissue oxygenation by loss of red blood cells is detrimental to healing and increases the risk of infection and tissue dehiscence.<sup>21–23</sup> An immunomodulatory effect of allogenic blood transfusions to compensate for perioperative blood loss has been suggested as causative for postoperative wound infections,<sup>24</sup> but data on transfusions were not recorded in our database.

Smoking and comorbidity such as diabetes, cardiovascular disease, and lung disease were associated with surgical site infections and dehiscence of tissue and wounds, thus confirming previous reports.<sup>17,25–29</sup> Several pathogenetic mechanisms may be involved. Smoking, microvascular disease, and severe lung disease are known to cause peripheral tissue hypoxia,<sup>30,31</sup> which increases the risk of wound infection and dehiscence.<sup>32</sup> In addition, some studies suggest that hypoxia, smoking, and diabetes reduce collagen synthesis and oxidative killing mechanisms of neutrophils.<sup>33–37</sup>

In emergency surgery, peritonitis in terms of localized pus or diffuse peritonitis was a strong predictor of wound and tissue complications. As shown by others, wound infection is likely to occur when peritonitis with a large intraabdominal bacterial load and bacteriemia is present, despite intravenous antibiotics administered perioperatively.<sup>3,6,8,16,38,39</sup> Male gender was a risk factor for postoperative complications following emergency operations, too. Especially wound disruption and anastomotic leakage has been reported as being more frequent.<sup>18,40,41</sup> The reason is dubious but may be associated with a lesser collagen production and reduced wound-healing capacity in men.<sup>42,43</sup> Multiple operations predict wound and tissue complications as well,<sup>44</sup> presumably due to bacterial contamination of the wound and tissue and resuture of relatively avascular scar tissue of the fascia.<sup>45</sup>

In this study, we achieved a high validity of data through different prospective and retrospective validation procedures. These measures were taken as the validity of data in clinical databases collected on a routine basis is poor unless a rigorous validation procedure is employed.<sup>46</sup> The limitations of this study are that some data were not collected, such as the patient's height and weight and the transfusions provided; thus, it was not possible to control for factors that have been shown by others to be associated with wound complications.<sup>24,47</sup>

In conclusion, factors known to affect the process of tissue and wound healing, like smoking, diabetes, cardiovascular disease, lung disease, male gender, contamination of the surgical site, blood loss, and the operation itself, were independent predictors of wound and tissue complications. Our findings provide data for preoperative identification of patients with a high risk of postoperative tissue and wound complications. Further, development of clinical pathways would prove valuable if the absolute risk of each patient could be estimated when planning surgery to specifically



optimize the patient's preoperative condition to reduce the risk of complications.

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